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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,225	07/28/2000	William W. Bachovchin	TUU-P01-006	3405

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/628,225	BACHOVCHIN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-42 and 46-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-42 and 46-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claim 42 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure of the cause of the glucose intolerance recited in instant claim 42. Applicants cite to page 51, line 6, of the specification as support for the amended claim limitation. The citation in the specification is limited to mice, and there is no indication that a GLP-1 receptor gene deletion or disruption exists in glucose intolerant animals in general. Finally, it is not clear, from the brief summary of the article given in the specification, that the article supports both deletion and disruption of the gene encoding the receptor. In general, disclosure of a species (e.g., just mice, or just gene deletion, or just gene disruption) does not constitute adequate written descriptive support for newly presented claims drawn to a genus encompassing the species.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 38-41 and 46-68 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of U.S. Patent No. 6,803,357 (which issued based upon copending Application No. 09/601,432). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '357 patent anticipate the instant claims.

5. Claims 38-41 and 46-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39, 40, 43-64, 66-78, 81-101, 103, 105-116, 119-121, 129-131, and 133-143 of copending Application No. 10/190,267. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '267 application anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 38-42 and 46-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-90 of copending Application No. 10/794,316. Although the conflicting claims are not identical, they are not patentably distinct from each other. The '316 application claims administering the same protease inhibitors to the same patients, claims that the protease inhibitors have an EC_{50} for modifying glucose metabolism which is at least one order of magnitude less than there EC_{50} for immunosuppression, and claims administering the protease inhibitors in amounts such that immunosuppression does not occur.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. The effective filing date of instant claims 38-41 and 46-68 is deemed to be February 2, 1998, the filing date of provisional application 60/073,409. Instant claims 38-41 and 46-68 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of the parent provisional application because the parent provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed invention.

8. Claims 38-40, 46-53, and 68 are rejected under 35 U.S.C. 102(e) as being anticipated by Villhauer (U.S. Patent No. 6,011,155). Villhauer teaches treating non-insulin-dependent diabetes, i.e. Type II diabetes, and increasing glucose tolerance by administering a DPIV inhibitor having the same structure as Applicants' page 9, line 7 - page 11, line 10. The inhibitors improve early insulin response to oral glucose challenges. Oral administration of the inhibitors is taught. Daily amounts preferably range from 1-100 mg, and oral administration can be 1-3 times/day. Treatment begins with small doses which are then increased until side effects arise. See, e.g., the Abstract; column 9, lines 48-65; and column 10, lines 28-47. In view of the relatively small doses which are preferred by Villhauer, in view of Villhauer's teaching to begin with small doses of the DPIV inhibitor so that side effects are avoided, and in view of the lack of any reported immunosuppressive side effects in Villhauer, Villhauer is deemed inherently to administer DPIV inhibitors in amounts such that glucose metabolism is modified while not suppressing the immune system of the patient being treated. With respect to instant claims 38-40 and 47-50, in view of the similarity in structure and function between the DPIV inhibitor of Villhauer and Applicants' disclosed DPIV inhibitors, the EC50's and Ki for the DPIV inhibitors of Villhauer will inherently be the same as is recited in instant claims 38-40 and 47-50. Sufficient evidence of similarity is deemed to be present between the DPIV inhibitors and

treatment methods of Villhauer and the inhibitors and methods recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors and methods are unobviously different than the DPIV inhibitors of Villhauer. With respect to instant claim 40, because the same active agents are being administered to the same animals according to the same method steps, inherently peptide hormone metabolism will be modified to the same extent in the method of Villhauer as is claimed by Applicants.

9. Claims 38-40, 46-53, and 68 are rejected under 35 U.S.C. 103(a) as being obvious over the German Patent 196 16 486. The German Patent '486 teaches using DP IV inhibitors to inhibit degradation of gastric inhibitory peptides and glucagon-like peptides, which effect can be used to reduce blood sugar levels and to treat diabetes mellitus. Inhibitors include alanyl pyrrolidide, isoleucyl thiazolidide, and N-valyl prolyl, O-benzoyl hydroxyl amine, and they can be administered orally. See, e.g., pages 1-2; page 10, line 21 - page 11, line 1; and page 11, line 15; of the attached translation. In view of the similarity in structure and function between the DPIV inhibitors of the German Patent '486 and Applicants' disclosed and claimed DP IV inhibitors, the EC_{50} and K_i values for the DP IV inhibitors of the German Patent '486 will inherently be the same as those recited in the instant claims. Sufficient evidence of similarity is deemed to be present between the DP IV inhibitors of the German Patent '486 and the inhibitors recited in Applicants' claims to shift the burden to Applicants to provide evidence that their inhibitors are unobviously different than those of the German Patent '486. The German Patent '486 does not teach administering its DPIV inhibitors in a single dose in amounts less than 2000 mg. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal dosages and dosage schedules for the

method of the German Patent '486 because dosage schedules are routinely determined and optimized in the pharmaceutical arts, and because it is desirable to minimize the number of administrations which are necessary for patient convenience and patient compliance. The German Patent '486 does not teach administering its DPIV inhibitors in amounts such that glucose metabolism is modified but the immune system of the patient being treated is not suppressed. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal doses for the treatment of the German Patent '486 because dose is an art-recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to minimize the amount of DPIV inhibitor administered to the patients in the German Patent '486 because it is routine in the art to minimize doses so as to minimize side effects.

10. Applicant's arguments filed March 23, 2005 have been fully considered but they are not persuasive.

The rejection of claim 42 under 35 U.S.C. 112, first paragraph, is maintained. Applicants' citations to page 4, lines 30-31, of the translation of the Gallwitz et al article cited in the specification, and to the De Ore et al article and the Ahren et al article attached as exhibits to the response, are noted. However, none of these references disclose the causes of glucose intolerance recited in claim 42, i.e. none disclose deletion or disruption of the gene encoding a glucagon type peptide 1 receptor in animals. While the effects of GLP-1 on glucose intolerance might be well-known, the issue is whether the claimed causes of glucose intolerance were possessed by Applicants and disclosed in their specification. While the prior art might suggest

that any disruption of the GLP-1 receptor will affect glucose intolerance, suggestion is not the test for written description under 35 U.S.C. 112, first paragraph.

The anticipation rejection based upon Villhauer (U.S. Patent No. 6,011,155) is maintained. Villhauer teach treating glucose intolerant animals - see, e.g., the Abstract, last three lines ("and further conditions of impaired glucose tolerance"), and column 10, lines 14-17 ("led to an improvement in glucose tolerance in the insulin resistant test animals"). Further, Villhauer teaches treating diabetic animals, which by definition are glucose-intolerant animals. Accordingly, in general terms and in the specific example involving Sprague-Dawley rats cited by Applicants, Villhauer teaches the treatment of glucose intolerant animals.

The obviousness rejection based upon the German Patent 196 16 486 is maintained. The declaration by Drucker under 37 CFR 1.131 filed April 22, 2004 and the declarations by Bachovchin and Plaut under 37 CFR 1.131 filed August 30, 2004 are not sufficient to antedate the German Patent '486 for the reasons of record. While section 4 of the Plaut Declaration, including Exhibit C, and section 4 of the Drucker declaration, established that the batch of Pro(boro)Pro was sent to Drucker in Canada, the cited sections of the declarations do not state that the experiments were carried out in this country, a NAFTA country, or a WTO country. The inference which Applicants' attorney attempts to make is not a satisfactory substitute for a statement which must occur in a declaration under 37 CFR 1.131. See MPEP 715.07(c): "The 37 CFR 1.131 affidavit or declaration must contain an allegation that the acts relied upon to establish the date prior to the reference or activity were carried out in this country or in a NAFTA country or WTO member country. See 35 U.S.C. 104." Applicants contend that the commencement of the OGTT experiments prior to October 1997 constitutes an actual reduction

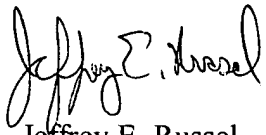
to practice of the present invention, and therefore there is no need to establish diligence. The examiner does not agree that the mere commencement of an experiment constitutes an actual reduction to practice. Actual reduction to practice requires that the claimed result be achieved and realized by the inventors (see MPEP 715.07 and 2138.050), and this can not occur immediately upon beginning an experiment. It may not take very long for the inventors to achieve and realize their claimed results, but it will take a finite amount of time, and neither Applicants' attorney nor the examiner can infer how much time this took and conclude that that reduction to practice occurred before the critical date of the reference. Only the affidavit or declaration under 37 CFR 1.131 can allege and establish reduction to practice prior to the critical date of the reference.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

May 4, 2005